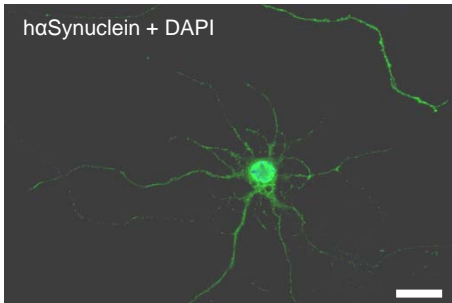


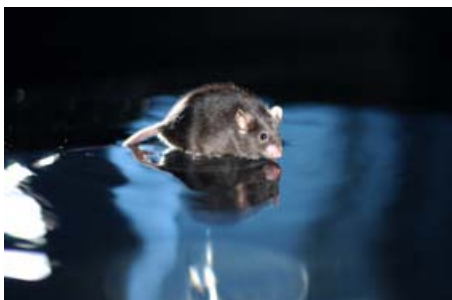
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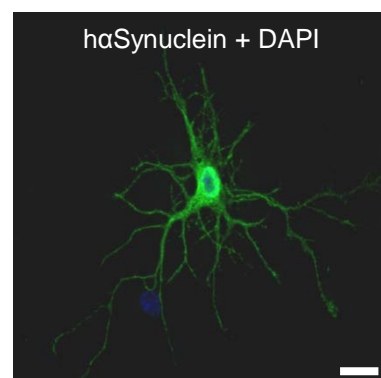
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TAU and alpha synuclein transgenic or transfected cells!

JSW Lifesciences provides numerous transgenic in vivo models including Tau and alpha-synuclein over-expressing mice to mirror disease related pathologies. To allow a better comparison between our in vitro and in vivo test systems, we continuously develop in vitro assays which are based on the already existing transgenic animal models.

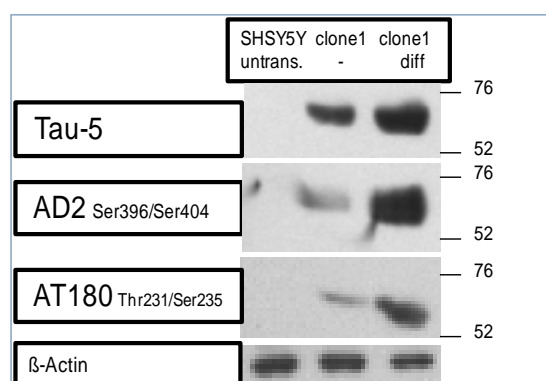
Here, we have established embryonic cortical cultures from transgenic mice over-expressing human wildtype alpha-synuclein under the control of the PDGF promoter. In these cultures, neurons produce ectopic human wildtype alpha-synuclein, which is detected in both cell soma and neuronal processes. Individual cortical neurons can be analyzed for various parameters in cultures with low cell density including:

- Levels of human wildtype alpha-synuclein
- Phosphorylated alpha-synuclein
- Subcellular localization of human wildtype alpha-synuclein
- Apoptosis related markers and cell signaling pathways



Besides the use of primary cultures derived from transgenic animals, JSW Lifesciences generated new neuronal cell lines stably transfected with disease related genes. Recently, we have developed a new SHSY-5Y cell line transfected with human Tau 441 bearing the missense mutations V337M and R406W under the control of the CMV promoter. Differentiated and undifferentiated SHSY-5Y cells highly over-express mutant Tau, which is phosphorylated at several disease-related epitopes. These cells can be analyzed for:

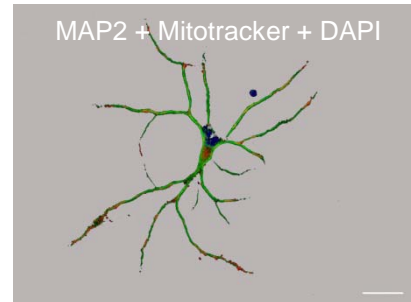
- Levels of human mutant Tau
- Various Tau phospho-epitopes including Thr231 and Ser396/404
- Cell signaling pathways



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In addition to analyzing protein levels in primary cultures and immortalized cell lines, the subcellular localization of proteins and organelles plays an important role in degenerating cells. In particular, mitochondria are at the center of attention as a reduction in mitochondrial activity has been strongly linked with various neurodegenerative diseases. Here, we demonstrate that mitochondria can be quantified according to their localization in somata or neurites in low density cultures of primary hippocampal neurons. The addition of toxins reduces the quantity of active mitochondria in neurites and soma. This analysis using specific dyes or immunolabelings can be applied for:

- Intracellular localization of proteins
- Localization of vesicles
- Localization of organelles (mitochondria, lysosomes, etc.)











Join us at the ICAD 2010 in Hawaii!

In nearly one week the ICAD 2010 begins, and JSW Lifesciences will join the ICAD to meet researchers, physicians and care providers from around the world. We are looking forward to this event.

So if you would like to get the newest information in the field of AD, PD, Huntington a.s.o. do not hesitate and join us at our boot no. 615 (...and pick up a little surprise which you can use immediately in Hawaii).

Manfred Windisch and his team would be pleased to welcome you!!!

































Behavioral testing

General health and motor ability tests are used to evaluate the effects of drugs, motor coordination, locomotor activity, hyperactivity, balance, exploratory behaviors and fatigue resistance on mice and rats.

- Irwin test (incl. various reflex tests)
- Pole test
- Challenging beam walk
- Grip strength test
- Rear climbing test
- Poke hole test



The **rotarod** apparatus is used to measure fore- and hind limb motor coordination and balance. The time a mouse is able to keep on an accelerating Rod is measured automatically by infrared light beams.



The most standardized general measure of locomotor function is spontaneous activity in the **open field** paradigm. The activity of the animal is automatically detected by infrared light beams in a 46x46cm transparent box.



Beam walk This test is a measure of motor coordination, particularly of the hind limbs where mice have to traverse an elevated narrow beam which is suspended between a start platform and their safe home cage. The time to fulfill the criterion and the number of foot slips is recorded.

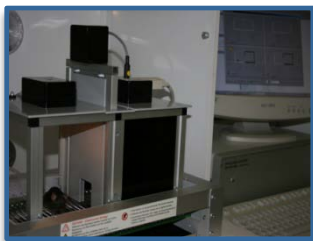
Memory and learning tests are used to evaluate spatial memory but also non-spatial memory associated with motivational cues (classically food).

- New object recognition task
- Two choice swim test
- T-Maze

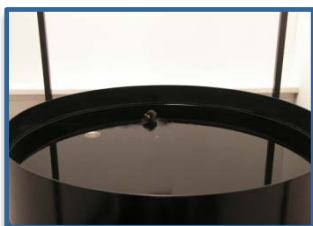


Contextual fear conditioning

On the training day mice receive a total of two CS/US package (tone /foot shock). Contextual memory is tested 24 hours after training. The mouse is placed into the same training chamber. Cued memory is done one hour after the contextual test in a novel chamber after some time of orientating the mouse receives the cued stimulus. Conditioning is assessed by scoring freezing behavior.



The aim of the **passive avoidance test** is learning to abstain from a particular response in order to avoid a punishing or aversive stimulus. The passive avoidance behavior based on negative reinforcement is recorded to examine long-term memory and emotional learning. The passive avoidance experiment is divided into two parts: Learning and testing. For learning the mouse is placed into the illuminated compartment. When the mouse enters the dark compartment the door will close and an electric stimulus takes place lasting for 2 seconds. For testing the mouse is placed into the illuminated compartment. The time until the mouse visits the dark box is measured.



The **morris water maze** is widely used to study spatial memory and learning. Animals are placed in a pool of water, where they must swim to a hidden escape platform. Each mouse has to perform three trials on each of four consecutive days. One hour after the last trial on day 4, mice have to fulfill a so-called probe trial. During the probe trial, the platform is removed from the pool and the number of crossings over the former target position is recorded together with the abidance in this quadrant.



Radial arm water maze It has similarities to the Morris Water Maze and to the radial-arm maze task but it uses weak aversive stimulation rather than more strong aversive stimuli such as food deprivation.

Animal **tests of anxiety and depression** are used to screen novel compounds for anxiolytic or anxiogenic activity, to investigate the neurobiology of anxiety, and to assess the impact of other occurrences such as exposure to predator odors or early rearing experiences.

The **forced swim test (FST)** is based on the assumption that animals will normally try to escape from an aversive stimulus. FST measures the time spent swimming versus the time spent floating in a tall cylinder filled with water. Animals are placed in a transparent Plexiglas cylinder filled with water for a 5 minute lasting test session. The behavior is videotaped and the duration of immobility as well as struggling and swimming during the whole 5 minutes session is calculated using an automated system.

The **elevated plus maze (EPM)** is a rodent model of anxiety that is used as a screening test for putative anxiolytic compounds/anxiogenic compounds and as a general research tool in neurobiological anxiety research. The test setting consists of a plus-shaped apparatus with two open and two enclosed arms, each with an open roof, elevated 50 cm from the floor. The model is based on rodents' aversion of open spaces. This aversion leads to the behavior termed thigmotaxis, which involves avoidance of open areas by confining movements to enclosed spaces or to the edges of a bounded space. The time spent in the open or closed arms is measured automatically by a video tracking system.